REMARKS

Claims 1-14, 17, 67, 68, and 70-94 were previously pending in this application. Claims 73-94 have been withdrawn from consideration by the Examiner as being directed to a non-elected invention, and are presently canceled without prejudice or disclaimer. As a result claims 1-14, 17, 67, 68, and 70-72 are pending for examination with claim 1 being an independent claim. No new matter has been added.

Applicants respectfully request reconsideration of claims 1-14, 17, 67, 68, and 70-72.

I. Claims 1-6, 12-14, 17, 67, 68 and 72 are Each Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey

Applicants traverse the rejection of claims 1-6, 12-14, 17, 67, 68 and 72 under § 103(a) over Kallioniemi (US 2002/0132246 A1), McGill (US 5,658,730), Pollack (Nature Genetics, vol. 23, pp. 41-46, September 1999), in view of GibcoBRL Catalog (pages 18-15 and 18-16, 1995-96) and Mackey (Anal. Biochem., vol. 212, pp. 428-435, 1993). As discussed further below, the above citations do not render any of claims 1-6, 12-14, 17, 67, 68 and 72 obvious.

A. The Scope of the Term "About" is Clear in view of the Specification

It is improper to interpret the term "about" to mean any number of bases. *See* page 2, lines 16-19 of the Final Office Action. It is well established that terms such as "about" are interpreted with reference to what a person of ordinary skill in the art would understand in light of the specification. (*See* MPEP § 2173.05(b).) The meaning and scope of such terms are intended to be flexible and can vary based on the context of their usage. In addition, under no situation would the term "about" be interpreted to include any number of bases as erroneously proffered.

Notwithstanding the above, the numerous embodiments in the specification provide guidance and shed light on the flexible meaning and scope of the term "about," as that term is used in relation to the number of bases in a nucleic acid fragment. For

example, Par. No. [0006], indicates the term "about" to mean a range other than "any number of bases."

> In other embodiments, the sample of target genomic nucleic acid is further prepared, e.g., fragmented, using procedures comprising mechanical fragmentation, e.g., shearing, or, enzymatic digestion, e.g., DNase enzyme, or equivalent, digestion, of a genomic nucleic acid (including the labeled nucleic acid generated by nick translation, random priming or amplification) to sizes smaller than about 200 bases, or, smaller than fragments of about 175 bases; about 150 bases; about 125 bases; about 100 bases; about 75 bases; about 50 bases; about 40 bases; about 30 bases; or about 25 bases. In another embodiment, the sample of target genomic nucleic acid (including the labeled target nucleic acid generated by nick translation, random priming or amplification) is prepared using a procedure comprising fragmentation of a genomic DNA to sizes smaller than about 200 bases by applying shearing forces sufficient to fragment genomic DNA followed by DNase or equivalent enzyme digestion of the sheared DNA to sizes smaller than about 200 bases, or, smaller than fragments of about 150 bases; about 125 bases; about 100 bases; about 75 bases; about 50 bases; about 40 bases; about 30 bases; or about 25 bases.

As described in Par. No. [0006], the number of bases of the nucleic acid fragments have a lower limit of about 25 bases and an upper limit of about 200 bases. In view of the above, it is improper to interpret "about" to mean any number of bases.

In addition, only claims 10 and 11 recite the term "about." Thus, this rejection cannot apply to the other pending claims.

B. Claims 1-6, 12-14, 17, 67, 68 and 72 are Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey

Applicants disagree that claims 1-6, 12-14, 17, 67, 68 and 72 would have been obvious to one of ordinary skill in the art over the Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey. The rejection is improper because no proper *prima facie* case of obviousness has been properly established. There is no teaching, suggestion or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention. (MPEP § 2143.) Moreover, even if proper evidence had been provided, any *prima facie* case of obviousness is rebutted because the teachings of Kallioniemi, McGill,

Pollack, GibcoBRL Catalog and Mackey fail to disclose, teach or suggest the method recited in claim 1.

One skilled in the art would not have been motivated to modify Kallioniemi or to combine Kallioniemi with any of the above citations. Kallioniemi does not disclose, teach or suggest a method that uses, in part, a plurality of immobilized nucleic acid segments in an array that are a collection of clones that represent all of a chromosome or a genome of an organism, and contacting such probes with labeled fragments that include both strands of a double-stranded genomic DNA, as claimed by Applicants.

In contrast to Applicants' claims, Kallioniemi describes a genosensor that scans the human genome for large deletions or duplications *in a single assay*. (emphasis added, Kallioniemi at page 14, Par. No. [0152], [0153].) Scanning the human genome using a genosensor *in a single assay*, as disclosed in Kallioniemi, is not the same as a method that uses a plurality of immobilized nucleic acid segments *in an array* that are a collection of clones that represent all of a chromosome or a genome of an organism as defined by claim 1.

There is also no disclosure, teaching or suggestion in Kallioniemi of the "observing" step of claim 1. In particular, Kallioniemi fails to disclose, teach or suggest an amount and location of labeled genomic nucleic acid hybridized to each immobilized probe, to detect regions of amplification or deletion in the sample, wherein positional information of clones on the arrays and chromosomes is correlated, thereby generating a molecular profile of the chromosome or genome of the sample genomic nucleic acid. Instead, Kallioniemi discloses revealing "the relative concentration of each target specific sequence in the probe mixture." (Kallioniemi at page 15, Par. No. [0157].)

Moreover, as acknowledged in the Office Action, Kallioniemi does not disclose, teach or suggest nucleic acid fragments with length of less than about 200 bp to less than about 30 bp. (*See* Final Office Action dated November 15, 2007 at page 6, Par. B.) Claim 1 recites, in part, that each genomic nucleic acid fragment consists of a length smaller than 200 bases.

The above-noted deficiencies of Kallioniemi are not cured by any of the secondary citations. In addition, the Examiner has not properly articulated a finding that there was some teaching, suggestion, or motivation, either in the references themselves or

in the knowledge generally available to one of ordinary skill in the art to modify the references. (MPEP § 2143.)

McGill does not disclose, teach or suggest contacting the immobilized probes with a sample of target nucleic acid comprising fragments of genomic nucleic acid, wherein said fragments include both strands of a double-stranded genomic DNA fragment and include at least 30% repetitive sequences, and wherein each labeled fragment consists of a length smaller than 200 bases. McGill, at best, provides ambiguity in the appropriate length for labeled fragments. McGill discloses different preferred or optimal labeled fragment lengths. For example, McGill states that, "it is contemplated that a nucleic acid fragment of almost any length.... For example, nucleic acid fragments may be prepared in accordance with the present invention which are up to 10,000 base pairs in length, with segments of 5,000 or 3,000 being preferred and segments of about 1,000 base pairs in length being particularly preferred." (McGill at col. 7, lines 31-40.) Thus, the teachings of McGill are contradictory as to what particular probe length is suitable. Because McGill does not clearly disclose the particular size of the labeled genomic nucleic acid fragments recited in claim 1, McGill, either alone or in combination with Kallioniemi, does not render the method of claim 1 obvious.

There also is no suggestion or motivation in McGill to combine McGill with Kallioniemi to arrive at the method of claim 1. McGill discloses diagnostic techniques for the detection of human prostate cancer. (*See* McGill Abstract.) No objective evidence has been provided that a person of ordinary skill in the art would be motivated to combine the molecular profiling method of Kallioniemi with the prostate cancer diagnostic techniques of McGill.

There also is no motivation to combine the teachings of Pollack with the teaching of Kallioniemi. Neither the Abstract nor page 46, first paragraph of Pollack discloses, teaches, or suggests the particular labeled nucleic acid fragment size recited in claim 1. Pollack does not disclose using labeled genomic nucleic acid smaller than about 200 bases. Therefore, even if Pollack is properly combinable with Kallioniemi, the combination is still deficient and does not render claim 1 obvious.

With reference to the assertion that Mackey provides the motivation to combine Kallioniemi, McGill and Pollack, this assertion is improper. It is well accepted that the

desirability of combining the cited references must exist in the cited references themselves. The mere fact that cited references can be combined or modified does not render the resultant combination obvious unless the results would have been predictable to one of ordinary skill in the art. (*KSR International Co v. Teleflex Inc.*, 550 U.S. __, __, 82 USPQ2d 1385, 1396 (2007); *see also* MPEP § 2143.01.)

The GibcoBRL Catalog was cited by the Examiner for the sole purpose of labeling. This purpose does not cure the deficiencies noted above.

Because no suggestion or motivation exists, either in the citations themselves or in the knowledge generally available to one of ordinary skill in the art, to modify Kallioniemi or to combine Kallioniemi with the secondary citations, and because Kallioniemi, either alone or combination with the secondary citations, does not teach or suggest all the claim elements of claim 1, no *prima facie* case of obviousness has been established.

Claims 2-6, 12-14, 17, 67, 68 and 72, which depend directly or indirectly from independent claim 1, are patentable for at least the same reasons as claim 1.

In view of the above, 1-6, 12-14, 17, 67, 68 and 72 are patentable over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey.

II. Claims 7, 8 and 10 are Each Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey, and further in view of Anderson

Claims 7, 8 and 10 stand erroneously rejected under § 103(a) over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey and further in view of Anderson (Nucl. Acids Res., vol. 9, pp. 3015-3027, 1981).

As discussed above, Kallioniemi, either alone or in combination with any of the listed secondary citations, does not render claim 1 obvious. Because claims 7, 8 and 10 each depend directly or indirectly from claim 1, Kallioniemi, either alone or in combination with any of the listed secondary citations, does not render claims 7, 8 or 10 obvious, for at least the same reasons as those stated above. Additionally, because the motivation to combine teachings of different citations must exist in the citations, or be

ascertainable therefrom, it is improper to use Anderson as the motivation to combine Kallioniemi, McGill, Pollack and Mackey. (*See* MPEP § 2143.01.)

In view of the above, no proper combination of citations has been provided to render obvious the method of claim 7, which further defines the method of claim 1 by specifying that the sample of target genomic nucleic acid is prepared using a procedure such as random priming, nick translation, and amplification to generate segments of target genomic nucleic acid; followed by a step comprising fragmentation or enzymatic digestion, or both, to generate a sample of target genomic nucleic acid consisting of sizes smaller than 200 bases. Similarly, claim 8 is not obvious in further defining the method of claim 7 by reciting that the random priming, nick translation, or amplification of target genomic nucleic acids incorporates detectably labeled base pairs into the segments. Also, claim 10 is not obvious in that it further defines the method of claim 1 to comprise prior to step (b), the step of fragmenting the sample of target genomic nucleic acid to sizes smaller than about 200 bases by DNase enzyme digestion.

For argument's sake, even if some motivation or suggestion to combine the citations did exist, Anderson still does not cure the deficiencies of Kallioniemi, McGill, Pollack, GibcoBRL or Mackey. Specifically, Anderson does not disclose fragmentation of target genomic DNA that has both strands labeled with a detectable moiety. Instead, the agarose gel shown in Figure 1 of Anderson was obtained by digesting lambda DNA with DNase I. There is no disclosure that both strands of the lambda DNA have been labeled.

In view of the above, claims 7, 8 and 10 are patentable over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey and further in view of Anderson.

III. Claim 9 is Patentable over Kallioniemi, McGill, and Pollack, in view of GibcoBRL Catalog, and Mackey, in view of Anderson, and further in view of Waggoner

Claim 9 stands erroneously rejected under § 103(a) over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey, in view of Anderson, and further in view of Waggoner (US 5,268,486).

As discussed above, Kallioniemi, either alone or in combination with any of the listed secondary citations, does not render claim 1 obvious. Because claim 9 depends indirectly from claim 1, Kallioniemi, either alone or in combination with any of the secondary citations, does not render claim 9 obvious, for at least the same reasons as those stated above. Additionally, because the desirability of combining citations must exist in the citations themselves, or be ascertainable therefrom, it is improper to use Anderson as the motivation to combine Kallioniemi, McGill, Pollack and Mackey. (*See* MPEP § 2143.01.) In view of the above, no proper combination of citations has been provided that renders claim 9 obvious.

For argument's sake, even if some suggestion or motivation to combine the citations did exist, Waggoner still does not cure the deficiencies of Kallioniemi, McGill, Pollack, GibcoBRL or Mackey. In particular, Waggoner does not disclose labeling of both strands of genomic DNA and fragmentation or enzymatic digestion of the genomic DNA. Therefore, Waggoner's disclosure of Cy3 and Cy5 does not render claim 9 obvious.

In view of the above, claim 9 is patentable over Kallioniemi, McGill, Pollack, in view of Gibco BRL Catalog and Mackey, in view of Anderson, and further in view of Waggoner.

IV. Claim 11 is Patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog, and Mackey, in view of Anderson, and further in view of Ordahl and Anderson

Claim 11 stands erroneously rejected under § 103(a) over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey, in view of Anderson, as applied to claim 1 above, and further in view of Ordahl (Nucl. Acids Res., vol, 3, pp. 2985-2999, 1976) and Anderson.

Claim 11 depends indirectly from claim 1. As discussed above, Kallioniemi, either alone or in combination with any secondary citation, does not render claim 1 obvious. For at least the same reasons, Kallioniemi, either alone or in combination with any secondary citation, does not render claim 11 obvious. Claim 11 further defines the method of claim 1 by reciting that prior to step (b) in claim 1, the step of fragmenting the

sample of target genomic nucleic acid to sizes smaller than that about 200 bases is performed by applying shearing forces sufficient to fragment genomic DNA followed by DNase enzyme digestion of the sheared DNA.

In addition to the above noted deficiencies, Ordahl discloses a technique that produces DNA fragments of approximately 230 base pairs, whereas claim 11 recites fragmenting to produce sizes smaller than about 200 bases by shearing followed by enzymatic digestion of the sheared DNA with DNase. Also, as discussed above in Section C, Anderson's disclosure of digesting lambda DNA with DNAse I is not sufficient, because there is no disclosure, teaching or suggestion that both strands of the lambda DNA have been labeled. Thus, no proper evidence has been provided that the combination of the citations necessarily discloses all elements that are recited in claim 11.

In view of the above, claim 11 is patentable over Kallioniemi, McGill, Pollack, in view of GibcoBRL Catalog and Mackey, in view of Anderson, as applied to claim 1 above, and further in view of Ordahl.

V. Conclusion

In view of the foregoing amendments and remarks, reconsideration is respectfully requested. This application should now be in condition for allowance; a notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 50/2762, (S2037-700210).

In view of the foregoing Amendments and Remarks, this application is in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes that the application is not in condition for allowance, the Examiner is invited to call Applicants' attorney at the telephone number listed below.

Respectfully submitted,
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